

**What is claimed is:**

1           1.     A device for manipulating a molecule *in vivo* relative to a target tissue  
2     comprising a support and at least one electrode member extending away from and affixed  
3     to or defining the support, the at least one electrode member having a plurality of  
4     conductive portions and a nonconductive portion, wherein:

5                 the conductive portions are positioned in spaced-apart relation from each  
6     other, each conductive portion being in circuit communication with a respective portion of  
7     a source of electrical energy;

8                 the conductive portions are configured to establish a first electromagnetic  
9     field between selected conductive portions sufficient to manipulate a molecule relative to  
10    a target tissue and a second electromagnetic field sufficient to cause transient permeability  
11    of a cell membrane within the target tissue; and

12                at least two of the conductive portions are locatable against a selected  
13    portion of the target tissue.

1           2.     The device recited in Claim 1, wherein the conductive portions and the  
2     nonconductive portion are located on a single support member.

1           3.     The device recited in Claim 1, wherein the conductive portions and  
2     nonconductive portion are located on separate support members.

1           4.     The device recited in Claim 1, wherein the electrode member comprises a  
2     plurality of electrode members affixed to the support and the conductive portions and the  
3     nonconductive portions are located along the electrode members.

1           5.     The device recited in Claim 1, wherein the conductive and the nonconductive  
2     portions comprise even pairs thereof.

1           6.     The device recited in Claim 1, wherein the conductive and the nonconductive  
2     portions comprise uneven pairs thereof.

1           7.     The device recited in Claim 1, wherein the support comprises a generally  
2     cylindrical post having a portal therethrough from a top end to a bottom end and the device  
3     further comprises:

4                 a disc affixed to the post bottom end, the disc having a bottom surface having  
5     an outer downwardly depending annulus comprising alternating sectors of conductive and  
6     nonconductive areas, the electrode member comprising the annulus and the conductive  
7     portions comprising the conductive sectors; and

8                 a lead in circuit communication with each conductive area and extending from  
9     the disc through the post portal to the top end thereof.

1           8.     The device recited in Claim 7, wherein the disc has a noncircular shape.

1           **9.**     The device recited in Claim 7, further comprising:  
2                     a plurality of contact means positioned adjacent the post portal top end and  
3     in circuit communication with each lead; and  
4                     interface means positioned adjacent the post portal top end having means  
5     for communicating with each contact means for establishing circuit communication with a  
6     signal generator.

1           **10.**    The device recited in Claim 9, wherein:  
2                     each of the contact means comprises a contact brush affixed within the portal  
3     against an inner wall thereof; and  
4                     the interface means comprises a key interlock insertable within the portal at  
5     the top end thereof and having a contact pad positioned for communication with each  
6     contact brush.

1           **11.**    The device recited in Claim 7, wherein the disc comprises a flexible material  
2     for permitting shape adaptation with the selected portion of the target tissue.

1           **12.**    The device recited in Claim 7, wherein the disc comprises a portion having  
2     sufficient transparency to permit visualization of the target tissue selected portion  
3     therethrough.

1           **13.**   The device recited in Claim 1, further comprising means for delivering a  
2           preselected pattern of signals to selected pairs of the conductive portions to effect a  
3           desired molecular result.

1           **14.**   The device recited in Claim 13, wherein the conductive and nonconductive  
2           portions comprise even pairs thereof.

1           **15.**   The device recited in Claim 13, wherein the conductive and nonconductive  
2           portions comprise uneven pairs thereof.

1           **16.**   The device recited in Claim 1, further comprising a downwardly depending  
2           post affixed adjacent a bottom end of the support, the post having at least one conductive  
3           area on a surface thereof.

1           **17.**   The device recited in Claim 16, wherein the downwardly depending post has  
2           a plurality of conductive portions thereon.

1           **18.**   The device recited in Claim 17, wherein the conductive and the  
2           nonconductive portions comprise even pairs thereof.

1           **19.**   The device recited in Claim 17, wherein the conductive and the  
2           nonconductive portions comprise uneven pairs thereof.

1           **20.**    The device recited in Claim 16, wherein the downwardly depending post has  
2 a single conductive portion thereon comprising an electrode.

1           **21.**    The device recited in Claim 20, wherein the post comprises a plurality of  
2 downwardly depending posts, each post axially movable between a first position and a  
3 second position lower than the first position and biased to the second position, for  
4 achieving contact between each post and a target tissue surface.

1           **22.**    The device recited in Claim 21, wherein each post is affixed to the support  
2 in spring-loaded fashion.

1           **23.**    The device recited in Claim 21, wherein each post extends in a generally  
2 linear fashion from the distal end of the support.

1           **24.**    The device recited in Claim 21, wherein the posts are curved with respect to  
2 the distal end of the support.

1           **25.**    The device recited in Claim 16, wherein each post has a pointed conductive  
2 bottom tip, the tips disposed at a radially inwardly facing angle to each other, each post  
3 inwardly movable between a first position and a second position wherein the tips are closer  
4 together than in the first position, the second position for gripping tissue between the tips.

1           **26.**   The device recited in Claim 1, further comprising a pair of electrode-bearing  
2 members movably affixed to the support in separation-adjustable fashion, each electrode-  
3 bearing member comprising means for affixing at least one electrode thereto.

1           **27.**   The device recited in Claim 26, wherein each electrode-bearing member  
2 comprises an insulating plate, and wherein the electrode members comprise a plurality of  
3 electrodes affixed to an inward-facing surface of each plate, the plates configured to grip  
4 at least a portion of the target tissue therebetween.

1           **28.**   The device recited in Claim 1, further comprising means for establishing at  
2 least one pair of opposite-polarity voltages approximately simultaneously on a respective  
3 pair of conductive portions.

1           **29.**   The device recited in Claim 1, further comprising means for selectively  
2 activating each conductive portion in a predetermined pattern.

1           **30.**   The device recited in Claim 29, wherein the source of electrical energy  
2 comprises a signal generator and the activating means comprises software means in  
3 controlling relation to the signal generator.

1           **31.** The device recited in Claim 1, wherein the support has a lumen therethrough  
2 dimensioned for admitting a syringe needle thereinto to permit an introduction of a  
3 substance containing the molecule into the target tissue.

1           **32.** The device recited in Claim 1, further comprising a needle member  
2 depending from a bottom of the support, the needle member having a pointed tip and an  
3 opening adjacent the tip, the tip and the opening positioned beneath the electrode  
4 member, the needle member adapted to deliver a substance containing the molecule  
5 through the opening into the target tissue.

1           **33.** The device recited in Claim 1, further comprising means for facilitating  
2 attachment of the electrode member to the target tissue.

1           **34.** The device recited in Claim 33, wherein the facilitating means comprises a  
2 mechanical means.

1           **35.** The device recited in Claim 33, wherein the facilitating means is selected  
2 from a group consisting of a barb and surface roughness.

1           **36.** The device recited in Claim 33, wherein the facilitating means comprises a  
2 chemical means.

1           **37.**    The device recited in Claim 36, wherein the facilitating means is selected  
2           from a group consisting of bioadhesives and adhesives.

1           **38.**    A method for achieving a desired distribution and delivery of a molecule from  
2           an initial location into a target tissue, the method comprising the steps of:

3                   placing at least one electrode-bearing member containing areas of  
4           conductivity capable of having reverse polarities, generally adjacent, but in nonpenetrating  
5           fashion to, a surface adjacent a target tissue, each electrode in circuit communication with  
6           a respective portion of a source of electrical energy;

7                   establishing a first electrical potential between a pair of the areas of  
8           conductivity sufficient to cause electromigration of the desired molecule from the initial  
9           location toward the target tissue; and

10                   establishing a second electrical potential between a pair of areas of  
11           conductivity higher than the first electrical potential sufficient to cause electroporation in  
12           the target tissue for enhancing a movement of the desired molecule into a cell thereof.

1           **39.**    The method recited in Claim 38, wherein the establishing steps comprise  
2           establishing a series of first and second electrical potentials in a predetermined sequence  
3           of pulses.

1           **40.**    The method recited in Claim 38, further comprising the step of establishing  
2           a third electrical potential between a pair of areas of conductivity sufficient to cause



electromigration of the desired molecule from a location adjacent the target tissue through a pore in a cell membrane of the target tissue into an interior thereof.

**41.** The method recited in Claim 40, wherein the establishing steps comprise establishing a series of first, second, and third electrical potentials in a predetermined sequence of pulses.

**42.** The method recited in Claim 38, wherein the electrode members are configured to at least partially surround a surface projection or a projection within an orifice near a periphery of the target tissue.

**43.** The method recited in Claim 38, wherein the electromigration is effected to cause the molecule to be delivered beneath a skin layer.

**44.** A method for delivering a bioactive molecule from an initial location to a target tissue, the method comprising the steps of:

placing at least one electrode member having areas of conductivity of opposite polarities against a surface generally adjacent, but in nonpenetrating fashion to, a target tissue, each member bearing sections of reverse polarity, each electrode member being in circuit communication with a respective portion of a source of electrical energy;

7                   activating a pair of the areas of opposite polarity to achieve an  
8                   electromigration of the bioactive molecule from the initial location to a location adjacent the  
9                   target tissue; and

10                   activating a pair of the areas of conductivity to achieve electroporation of a  
11                   cell membrane within the target tissue sufficient to permit entry of the biological molecule  
12                   into the cell interior.

1                   **45.**    The method recited in Claim 44, wherein the electromigration is effected to  
2                   cause the molecule to penetrate a skin layer.

1                   **46.**    A method for bringing two molecules from two respective initial locations into  
2                   apposition at a desired target tissue site for permitting a reaction therebetween, the method  
3                   comprising the steps of:

4                   placing an electrode member containing at least two areas of conductivity  
5                   thereon against a surface adjacent a desired target tissue site;

6                   activating the areas of conductivity to cause an electromigration of the first  
7                   and the second molecule to a third area adjacent the target tissue site; and

8                   permitting the first and the second molecule to react at the third area.

1                   **47.**    The method recited in Claim 46, wherein the activating step comprises  
2                   establishing an electrical potential between the pairs of areas of conductivity sufficient to  
3                   cause the electromigration of the first and second molecule in a desired direction.

1           **48.**    The method recited in Claim 47, wherein the electromigration is effected to  
2           cause the first and the second molecule to penetrate a skin layer.

1           **49.**    The method recited in Claims 46, wherein the activation step causes the first  
2           and the second molecule to be delivered to an internal compartment or cytosol of cells  
3           comprising the target tissue.

1           **50.**    The method recited in Claim 46, wherein the penetration step is effected  
2           through a biological tissue other than skin.

1           **51.**    The method recited in Claims 46, wherein the activating step is sufficient to  
2           cause electromigration but is insufficient to cause electroporation.

1           **52.**    The method recited in Claim 46, further comprising the step, prior to the  
2           activating step, of activating the areas of conductivity to cause an electroporation of the  
3           target tissue.

1           **53.**    The method recited in Claim 46, wherein the electromigration is effected from  
2           a plurality of sides of the target tissue, and wherein the electrode member comprises a  
3           plurality of electrode members adjacent the target tissue.

1           **54.**    The method recited in Claim 53, wherein the electrode member comprises  
2           a plurality of electrode members, and wherein the activating step is sufficient to effect  
3           electromigration but is insufficient to effect electroporation.

1           **55.**    The method recited in Claims 46, further comprising the step, following the  
2           activating step, of activating the areas of conductivity sufficiently to cause electroporation  
3           in the target tissue.

1           **56.**    The method recited in Claims 46, further comprising the step, substantially  
2           simultaneously with the activating step, of activating the areas of conductivity sufficient to  
3           cause electroporation in the target tissue.

1           **57.**    A method for making a molecule electromanipulator comprising the steps of:  
2                    affixing at least one member containing areas of discrete conductivity to a  
3           support in spaced-apart relation, each area of conductivity being differentially activatable;  
4                    providing circuit communication between each conductivity area and a source  
5           of electrical energy, the conductive areas configured to establish a low-level  
6           electromagnetic field *in vivo* between selected conductivity areas for manipulating a  
7           molecule relative to a target tissue and a higher-level electromagnetic field for causing  
8           transient permeability of a cell membrane within the target tissue; and

9 providing switching means between each conductivity area and the electrical  
10 energy source to permit differential activation of the areas of differing conductivity on each  
11 electrode member.

1 **58.** The method recited in Claim 57, further comprising the step of providing  
2 means for controlling the switching means adapted to activate the areas of conductivity in  
3 a preselected pattern.